REMARKS

Claims 1-33 are pending in the application. Claims 1-33 were rejected. No claims were allowed.

Applicants point out that their claim of foreign priority under 35 U.S.C § 119 was not acknowledged in the Office Action mailed March 28, 2006, although the Updated Filing Receipt mailed September 20, 1994, indicates receipt of foreign application India 308/MAS/2003. Applicants request that their claim of foreign priority be acknowledged in the next official communication issued by the Examiner.

The specification has been amended to correct an inadvertent transcriptional error in the paragraph beginning at line 16 of page 5. No new matter has been introduced by the amendment.

Claims 4, 14 and 20 have been amended to specify that the 2 theta values are in degrees. Support for the amendments can be found throughout the specification and claims as originally filed, *e.g.*, page 9, lines 16-19, page 13, lines 4-14 and claims 1-3, 13 and 19. Claim 33 has been amended to correct improper dependency from claim 28 to claim 32. Support for the amendment can be found throughout the specification as originally filed, *e.g.*, page 20, lines 11-30. No new matter has been introduced by the amendments.

Reconsideration and allowance of the rejected claims in view of the amendments above and the remarks below are respectfully requested.

Claim Rejections – 35 U.S.C. § 112

Claim 30 was rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. According to the Examiner, claim 30 is ambiguous because it is a method of treating claim dependent from a process of making claim 28. Further, according to the Examiner, there is no antecedent basis for the term "mammal" in claim 28. Applicants respectfully traverse this rejection.

Contrary to the Examiner's contention, claim 30 is not a method of treatment claim and does not recite the term "mammal." Rather, claim 30 is a product-by process claim that properly depends from claim 24, which is directed to a process for preparing

crystalline Form III of moxifloxacin monohydrochloride. Accordingly, reconsideration of this rejection is respectfully requested.

Applicants believe that the Examiner intended to reject method of treatment claim 33 under 35 U.S.C. §112, second paragraph, as improperly depending from claim 28. Claim 33 has been amended to depend from claim 32, which is directed to a method of treating infections in a mammal. Applicants submit that the amendment moots any rejection of claim 33 under 35 U.S.C. §112, second paragraph, that could be forthcoming.

Claim Rejections – 35 U.S.C. § 102

Claims 1-33 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Grunenberg (US 5,849,752). According to the Examiner, Grunenberg teaches a crystalline form of anhydrous moxifloxacin monohydrochloride with XRPD peaks similar to the peaks of the instantly claimed Form III. Further, according to the Examiner, if the instantly claimed Form III is different than the form taught by Grunenberg, the pharmaceutical compositions of claims 18-20 and 23 would appear to be same (inherently) because one pharmaceutical carrier is water, which causes loss of specific crystalline structure. Similarly, according to the Examiner, the method of treatment claims 32-33 would appear to be the same because crystalline forms of drugs are absorbed into the body through the bloodstream, whereupon they lose their specific crystalline structure. The process of claims 24-29, according to the Examiner, appears to be fully embraced by the process taught by Grunenberg. Applicants respectfully traverse this rejection.

With respect to claims 1-17, 30 and 31, Applicants submit that the instantly claimed crystalline Form III of anhydrous moxifloxacin monohydrochloride and the anhydrous moxifloxacin monohydrochloride taught by Grunenberg are indeed different.

Contrary to the Examiner's contention, even a cursory inspection of the X-ray powder diffraction patterns for the two forms shows they are distinctly different. For example, the pattern for the instantly claimed crystalline Form III shows a very prominent peak at 7.1° two theta that is completely absent from the pattern for the form taught by Grunenberg. Furthermore, the pattern for the instantly claimed crystalline

Form III shows several less prominent peaks at 10.0°, 12.2° and 13.1° two theta not present in the pattern for the form taught by Grunenberg. Because the instantly claimed crystalline Form III of anhydrous moxifloxacin monohydrochloride and the anhydrous moxifloxacin monohydrochloride taught by Grunenberg have different diffraction patterns, they are distinct molecular forms and Applicants submit that claims 1-17, 30 and 31 are not anticipated under § 102(b), and reconsideration of this rejection is respectfully requested.

With regard to claims 18-20 and 23, Applicants submit that reading the claims to encompass solutions where the pharmaceutical carrier is water and all crystalline structure is lost is contrary to the plain meaning of the claim language. Claims 18-20 and 23 specifically recite "crystalline Form III," meaning that moxifloxacin monohydrochloride in solution (and thus lacking a crystalline structure) is outside the scope of these claims. In contrast to the properly construed claims, Grunenberg does not disclose crystalline Form III of anhydrous moxifloxacin monohydrochloride, and thus does not disclose pharmaceutical compositions comprising the same. Accordingly, Applicants submit that claims 18-20 and 23 are not anticipated under § 102(b), and reconsideration of this rejection is respectfully requested.

With regard to claims 32 and 33, Applicants submit that Grunenberg does not teach a method of treating infections by administration of crystalline Form III of anhydrous moxifloxacin monohydrochloride. Although the Examiner may be correct that crystalline forms of drugs are absorbed into the body through the bloodstream, whereupon they ultimately lose their specific crystalline structure, those skilled in the art recognize that the specific form of a drug may affect its dissolution rate, solubility and bioavailability upon administration to the bloodstream, thereby affecting its therapeutic efficacy. For example, N. K. Jain and M. N. Mohammedi, *Indian Drugs*, Vol. 23, pages 315-329 (1986), a copy of which is provided herewith for the benefit of the Examiner, state at 315:

> The polymorphs show different solubilities and rates of solution, hence different absorption (bioavailability) tendencies.

Similarly, M. Rouhi, *Chemical & Engineering News*, Vol. 81, pages 32-35 (Feb. 24, 2003), an internet reprint copy of which is provided herewith for the benefit of the Examiner, reports on the third page:

> Different polymorphs differ in bioavailability, solubility, dissolution rate, chemical and physical stability, melting point, color, filterability, density and flow properties. . .

N. A. Muzaffar and M. A. Sheikh, *Journal of Pharmacy (Lahore)*, Vol. 1, pages 59-66 (1979), a copy of which is provided herewith for the benefit of the Examiner, give specific examples of drugs whose absorption and therapeutic efficacy are dependent upon their solid-state form. Because Grunenberg does not teach a method of treating infections by administration of crystalline Form III of anhydrous moxifloxacin monohydrochloride, Applicants submit that claims 32 and 33 are not anticipated under § 102(b), and reconsideration of this rejection is respectfully requested.

With regard to claims 24-29, Applicants submit that Grunenberg does not teach a process for preparing crystalline Form III of anhydrous moxifloxacin monohydrochloride. In fact, Grunenberg does not teach a process for preparing anhydrous moxifloxacin monohydrochloride at all. Rather, Grunenberg is concerned with the preparation of moxifloxacin hydrochloride monohydrate involving treatment of moxifloxacin hydrochloride with water. Grunenberg states at col. 1, ln. 66 to col. 2, ln. 25:

> The invention accordingly relates to the new monohydrate of CDCH of the formula I . . . and to a process for its preparation, which is characterized in that anhydrous, crystalline CDCH is treated with an amount of water sufficient for thorough mixing and for formation of the monohydrate at temperatures below 80° C. until the stoichiometric content of water of crystallization has been absorbed and conversion of the crystals is complete, and the crystals thus obtained are separated off and dried to the constant weight of the monohydrate in order to remove the adsorbed water present. To avoid the formation of the anhydrous form, the humidity during drying should be not less than 30% relative humidity. The monohydrate crystallizes in the form of needles from water-containing media with a water content of more than 10%. (Emphasis added.)

In contrast, claims 24-29 of the instant application recite two different methods for the preparation of crystalline Form III of anhydrous moxifloxacin monohydrochloride, involving either 1) refluxing azeotropically moxifloxacin monohydrochloride in a solvent selected from the group consisting of lower branched esters, chained acid esters, aliphatic ketones and aliphatic hydrocarbon solvents, and cooling the refluxed solvent while stirring the mixture until a solid separates (claims 24 and 25), or 2) dissolving moxifloxacin hydrochloride in a lower alkyl alcohol to obtain a solution, and adding to the solution an anti solvent, in which moxifloxacin hydrochloride is poorly soluble (claims 26-29). The final step of both methods involves isolating crystalline Form III of anhydrous moxifloxacin monohydrochloride.

Grunenberg does not disclose refluxing azeotropically moxifloxacin monohydrochloride in any solvent, let alone any of the solvents recited in claims 24 and 25, nor does Grunenberg describe adding an anti solvent to an alcoholic solution of moxifloxacin monohydrochloride as recited in claims 26-29. Further, as discussed above, Grunenberg does not disclose crystalline Form III of anhydrous moxifloxacin monohydrochloride. Because Grunenberg does not teach the preparation of crystalline Form III of anhydrous moxifloxacin monohydrochloride using either of the instantly claimed methods, Applicants submit that claims 24-29 are not anticipated under § 102(b), and reconsideration of this rejection is respectfully requested.

CONCLUSION

It is believed that claims 1-33 are in condition for allowance, and an early notice of allowability would be appreciated. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number indicated below to discuss the same.

Respectfully submitted,

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